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10/089,027	03/26/2002	William E. Jack	NEB-166-PUS	9409

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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
04/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/089,027	JACK ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-42* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment of claim 32, in the paper of 1/9/2009, is acknowledged. Claims 32-43 remain pending and at issue for examination.

Applicant's election of the species of SEQ ID NO: 5, in the paper of 2/11/2008, continues to be acknowledged.

Applicants' arguments filed on 1/9/2009, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 43 is objected to because of the following informalities:

Claim 43 is dependent on rejected claims 32 and 33. Applicant's comments regarding this objection are noted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as it applied to previous claims 32-42. In response to this rejection applicants have amended claim 32 and traverse the rejection as it applies to the newly amended claims.

Applicants note that the previous claims were entirely reworked in the prior submission and were disappointed that the prior rejection reiterated almost verbatim with little or no reference to the actual claim language. Applicants also have noted that they are disappointed that the presently levied rejection has not addressed what applicants feel are very differing claims in regard to scope. The examiner apologizes for any disappointment that applicants and their representative feel with the presentation of the previous rejection and will attempt to rectify this in the present office action.

Applicants continue to traverse the current rejection on the same basis that they have previously argued, that of the decision in Invitrogen Corp v. Clontech Labs 77 USPQ2d 1161 (Fed Cir 2005) supports applicants position that the current claims satisfy the description requirement.

In arguing applicants point, applicants note that previously the examiner pointed out to applicants that the two cases are different, a fact that applicants appreciate and acknowledge and applicants further point out that the examiner previously pointed out that unlike the Invitrogen case, the instant claims "are not drawn to a polypeptide product, but rather they are drawn to a method of use of a very broad

subgenus of DNA polymerases." Interestingly applicants assert that "the Examiner has it backwards". Applicants submit that the examiner correctly notes that the Invitrogen claims are drawn a polypeptide although applicants submit that the examiner is utterly incorrect in implying that the claims in the present case are more broad than those at issue in Invitrogen. Applicants submit that claims to a polypeptide are always broader than claims to a method of using the polypeptide. While applicants point that claims to a polypeptide are always broader than claims to a method of using the polypeptide is interesting, applicants attention is directed to the statements made in the previous office action. The examiner did not say nor was it implied that the claims of the instant application are broader than the claims in Invitrogen. The point that was being made is that the instant claims are not drawn to a polypeptide product, (as in Invitrogen) but rather the instant claims are drawn to a method of use of a very broad subgenus of DNA polymerases. No comparison was being made in this statement. As was previously stated following the above statement regarding the claims, the said subgenus of DNA Polymerases must be capable of incorporating acyclonucleotides into a primer extension reaction and while applicants have presented six examples of encompassed DNA polymerases, and required the inclusion of a 15-amino acid motif in that DNA polymerase of the claimed methods, it remains that applicants have not related the subgenus of structure to the acyclonucleotide incorporation function. This lack of description remains in spite of applicants arguments that the current claims are described as equally as those in the *Invitrogen* decision. For these reasons and those presented previously the rejection of the current methods is maintained.

With regard to applicants question, (1) how the DNA polymerase description in the present case differs from that in *Invitrogen* such that the written description requirement is satisfied in one case and not the other; applicants are reminded that applicants claimed methods require the incorporation of acyclonucleotides into a DNA. This is not a property of a DNA polymerase that is well known in the art and applicants have not adequately described this supposedly new function of a specific sub-genus of DNA polymerases. This is in contrast to the claims of Invitrogen in which the homologies of the encompassed DNA polymerases were high and that region responsible for the reduced RNAse H activity in each of these DNA polymerases known such that the encompassed DNA polymerase variants were known. Such is not the case regarding those DNA polymerases encompassed by the structural limitations of the instant claimed methods. Thus these methods of use of the referred to subgenus of DNA polymerases remains inadequately described.

With regard to applicants question, (2) on what basis does the Examiner justify limiting the claims in the present case to only those specifically exemplified embodiments when *Invitrogen* holds that much broader description is supported by much narrower exemplification, applicants are reminded that Invitrogen does not hold that a much broader description is supported by a much narrower exemplification. First the description held by Invitrogen is specific to the claims of invitrogen, based upon the specification and art as well as a. Actual reduction to practice, b. Disclosure of drawings or structural chemical formulas, c. Sufficient relevant identifying characteristics, such as: i. Complete structure, ii. Partial structure, iii. Physical and/or chemical properties, iv.

Functional characteristics when coupled with a known or disclosed correlation between function and structure, d. Method of making the claimed invention, e. Level of skill and knowledge in the art and f. Predictability in the art.

As discussed previously and above, applicants have not described a sufficient correlation between function and structure for the claimed sub-genus of methods of use of the necessary DNA polymerases, nor have applicants met any of the others means of description regarding applicants invention.

With regard to applicants question, (3) the specific rationale as applied to each pending claim, given the dramatic difference in scope of different claims, first applicants are reminded that the contrary to applicants submission, the different claims are not dramatically different in scope. While claim 33, requires a mere 70% identity to SEQ ID NO: 4, relative to the 30% identity of claim 32, the breadth of this genus remains inadequately described for all of the same reasons discussed previously and repeated above. Claims 34, 35, 36, 37, 38 and 40-42 each depend from claims 32 (having 30% identity to SEQ ID NO: 4) or 33 (having 70% identity to SEQ ID NO: 4) but require that the additional amino acid motif is selected from a smaller "group of amino acid motifs" and while these claims are narrower in that the single amino acid motif required of the DNA polymerase is selected from a different (smaller) group of amino acid motifs or the single motif is not able to be as varied as in claim 32, the breadth of the these claims is not significantly different from that of claim 32. Thus since applicants have not described the claimed methods of claim 32, the slight difference in breadth of claims

33-38 and 40-42 are not such that they would overcome the deficiencies of the necessary description of the claimed methods.

With regard to applicants discussion regarding previous Example 14 and the Written Description Guidelines, it is noted that these previous Examples and Guidelines for Written Description have changed. Applicants reference to previous Example 14, would now appear to correlate with Example 11 of those Written Description Guidelines presented on the USPTO website.

While applicants claims are not drawn to a nucleic acid as in Example 11, of the Written Description Guidelines, applicants claims are drawn to a method which requires a DNA polymerase which has 30% identity to a specific sequence an additional single amino acid motif and a specific function, that is the incorporation of acyclonucleotides into a DNA and thus for the purpose of guidance, claim 2 of Example 11 seems most appropriate. It is noted that claim 2 is drawn to a nucleic acid having 85% identity to a specific sequence, a partial structure. This is relative to the instant claims which require even less partial structure of 30% amino acid identity. Similar to claim 2 of Example 11 of the Guidelines, there is no teaching regarding which 70% of the amino acids may vary from SEQ ID NO: 4. Except for the existence of one of the 15 amino acid motifs selected from SEQ ID NO: 5-22 or variants thereof, which is relative to the protein encoded by the 5837 nucleotide SEQ ID NO: 4 (presumably around 800 amino acids) . This disclosure regarding the protein encoded by SEQ ID NO: 4 and the specific function of incorporating acyclonucleotides into a DNA template combined with the pre-existing knowledge in the art fails to satisfy the written description of 35 USC 112 first

paragraph. Further given the extreme breadth of claim 32, which requires that the referenced DNA polymerases maintain merely a 30% identity to that protein encoded by SEQ ID NO: 4, for all practical purposes, this claim requires next to no conservation of structure. Any additional minimal structure added by the dependent claims 33-38 and 40-42, is insufficient to describe a sufficient structure to functional correlation.

Thus for these reasons the rejection based upon a lack of written description is maintained as an art recognized structure-function correlation is not present.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 32-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising providing a DNA Polymerase selected from the group consisting of Vent, Deep Vent, *Pfu* and 9°NTM or the specifically disclosed variants referred to in claim 43, with a template, a primer that binds to the template and a nucleotide solution containing at least one acyclonucleotide and incubating the DNA polymerase with the template and the nucleotides so that the DNA polymerase extends the primer by incorporating the nucleotides, does not reasonably provide enablement for any method comprising providing a DNA Polymerase having an amino acid sequence that shows a mere 30% overall identity with that of SEQ ID NO: 4 and further includes a 15 amino-acid motif that is identical to SEQ ID NO: 5 except that it contains up to 3 amino acid substitutions as compared with

the SEQ ID NO, with a template, a primer that binds to the template and a nucleotide solution containing at least one acyclonucleotide and incubating the DNA polymerase with the template and the nucleotides so that the DNA polymerase extends the primer by incorporating the nucleotides The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as it applied to previous claims 32-42. In response to this rejection applicants have amended claim 32 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that applicants submit that the Examiner maintains this rejection without offering *any* explanation or support of this position.

Applicants submit that the incorporation of acyclonucleotides into a DNA involves incubating a DNA polymerase capable of incorporating acyclonucleotides with (1) a template; and (2) nucleotides and that thus, the only difference between what is claimed and what the art acknowledges is which DNA polymerase is used. Applicants submit that the present specification teaches that DNA polymerases with 30% overall identity with the polypeptide encoded by SEQ ID NO:4 and including a 15 amino acid motif identical to one of SEQ ID NOs 5-22 (except for having up to 3 amino acid substitutions) can incorporate acyclonucleotides. Thus, there can be no *enablement* challenge beyond the *written description* challenge. Applicants submission here is objected to on the basis that it appears to be misleading. Applicants do not teach that DNA

polymerases with 30% overall identity with the polypeptide encoded by of SEQ ID NO:4 and including a 15 amino acid motif identical to one of SEQ ID NOs 5-22 (except for having up to 3 amino acid substitutions) can incorporate acyclonucleotides but rather applicants teach that specific DNA polymerases which have as little as 30% identity to SEQ ID NO: 4 and also include a 15 amino acid motif selected from one of SEQ ID NOs 5-22 can incorporate acyclonucleotides. The identification of the species does not enable the breadth of the claimed genus.

Applicants submit that the specification makes clear that (1) all tested DNA polymerases having the motif have the activity; and (2) DNA polymerases lacking the motif do not. This argument presented by applicants is addressed below.

Applicants submit that the Examiner has indicated that claims to specifically exemplified species are allowable, and nothing more and it that it is a rare invention indeed whose contribution is bounded precisely by the data generated by the Applicant. In response to this argument it is acknowledged that applicants often are enabled to more than the specifically taught species, however, the claims as they currently exist and the supporting argument is not persuasive that these claims are enabled. Applicants further submit that upon applicants own search of the patent databases, Applicants have determined that many of the polymerase patents issued by Examiner Hutson are drawn to claims which reference 90% identity to a specific sequence and that applicants claims should not be held to this same standard 90% benchmark on the basis that applicants have further enabled the claimed methods with reference to additional structural motifs.

In response to this argument the examiner cannot comment on applicants presented "generalized trends" as these are not considered relevant to the enablement of the claims of the instant application.

Applicants complete argument continues to be acknowledged but not found persuasive for the reasons stated previously and repeated herein. It is admitted that the maintenance of the current enablement rejection may in part be due to applicants means of claiming applicants invention.

Without sufficient guidance, determination of those DNA polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In spite of applicants cited reasons, the rejection is maintained on the basis that applicants have not met applicants burden with regard to the Wands factors for the reasons previously stated.

It continues that applicants have not enabled the scope of the claimed methods on the basis that applicants have not given guidance as to those DNA polymerases which have the ability to incorporate acyclonucleotides into a DNA template. It is noted that applicants claims encompass not only methods of use of naturally occurring DNA polymerases, but also variants and mutants thereof. As discussed above and previously, applicants have merely identified a few specific DNA polymerases within the 30% sequence identity range that have the necessary acyclonucleotide incorporation

function. Such does not enable the breadth of the claimed subgenus of methods of use of the encompassed DNA polymerases which encompasses not only the use of naturally occurring DNA polymerases but also variants and mutants thereof. It remains that applicants have not enabled the extreme breadth of those DNA polymerases so encompassed. Applicants have not enabled the breath of those methods of incorporating acyclonucleotides comprising the use of those DNA polymerases having a mere 30% identity to that polypeptide encoded by SEQ ID NO: 4 and comprising a motif that is selected from the 18 different amino acid motifs listed in SEQ ID NOs: 5-22 and variants thereof.

With regard to applicants argument regarding the identification of an amino acid motif domain that is required for this specific function of acyclonucleotide incorporation, it is noted that applicants specification at page 19, lines 22-24, does not clearly support such. The clarification or expansion of applicants argument regarding this reference to "the motif" on page 8, line 7 of applicants argument submitted on 1/9/2009, might be helpful in overcoming this rejection if the referred to "the motif" is shown to correlate with the incorporation of acyclonucleotides. To date this showing has not been clearly established and as such applicants have not enabled the currently claimed methods beyond the taught species. One of the reasons it appears that applicants have not established a correlation between a motif and the acyclonucleotide incorporation function, appears that applicants have not disclosed such a single motif but rather continue to refer to any of a number of motifs or variants thereof.

Beyond the above, without sufficient guidance, determination of those methods and polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
4/14/2009

/Richard G Hutson/
Primary Examiner, Art Unit 1652